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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,432	10/27/2005	Svend Kaasgaard	10300.204-US	7515

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EXAMINER	
GOUGH, TIFFANY MAUREEN	
ART UNIT	PAPER NUMBER
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,432	KAASGAARD ET AL.	
	Examiner	Art Unit	
	Tiffany M. Gough	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 10/27/2006 has been received and entered into the case. Claims 1-13 have been cancelled and new claims 23-31 have been added. Claims 14-31 are pending and have been considered on the merits. All arguments and amendments have been considered.

Claim Rejections - 35 USC § 112

The previous 35 USC 112 first paragraph rejection is withdrawn.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 recites the limitation "1,3 ethylene glycol" depending on the method of claim 14. There is insufficient antecedent basis for this limitation in the claim. Claim 14 does not recite the compound 1,3 ethylene glycol. For examination purposes, it has been interpreted as ethylene glycol.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14-23,25,26,29,30 rejected under 35 U.S.C. 102(e) as being anticipated by Kaasgaard et al (US2004/0175812A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicant claims a method for fermenting a bacterium, specifically *Bacillus* sp., producing an enzyme of interest, specifically a hydrolase, in a culture medium of atleast 50 liters comprising adding one or more compounds in the amount of atleast 0.1%(w/w) selected from 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, mannitol, erythritol, cellobiose, sorbitol and a polyether having an average molecular weight less than 1000, either before and/or during fermentation. Applicant also claims addition of a salt to the medium, such as a chloride, sulphate, phosphate, nitrate, and ammonium salt. The enzyme of interest, a hydrolase, is recovered after removal of the bacterium.

Kaasgaard et al teach a method of recovering a protein of interest by the addition of compounds, specifically polyols and carbohydrates including, trehalose, xylitol, erythritol, sorbitol, monopropylene glycol,i.e. 1,2-propanediol to a bacterial fermentation medium during fermentation wherein an enzyme on interest is recovered (see abstract,0007-0009,0051-0057,0080-0096, claims 1-18) after the removal of the bacterium. They disclose the bacteria to be of the Bacillus genus and the enzyme to be a hydrolase (see 0007-0022). They also teach the addition of salts such as chloride, sulphate, phosphate, nitrate, and ammonium salt (see 0106-0108). The polyol is added in an amount of at least 0.1%(w/w) of medium (see 0093).

Although, Kaasgaard do not specifically disclose 1,2 and 1,3 propandiol, they do disclose monopropylene glycols. Propylene glycols, such as 1,2 propandiol are known in the art to be the collective name for monopropylene glycols, thus, 1,2 and 1,3 propandiols would inherently be covered by the term monopropylene glycol.

Therefore, the reference anticipates the claimed subject matter.

Claims 14-17,19-22,24 are rejected under 35 U.S.C. 102(b) as being anticipated by Brothers et al (U.S. Patent 4,673,647).

Applicant claims a method for fermenting a bacterium, specifically *Bacillus* sp., producing an enzyme of interest, specifically a hydrolase, in a culture medium of atleast 50 liters comprising adding one or more compounds in the amount of atleast 0.1%(w/w) selected from 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, mannitol, erythritol, cellobiose, sorbitol and a polyether having an average molecular weight less than 1000, either before and/or during fermentation. Applicant

also claims addition of a salt to the medium, such as a chloride, sulphate, phosphate, nitrate, and ammonium salt. The enzyme of interest, a hydrolase, is recovered after removal of the bacterium.

Brothers et al disclose a process for the recovery of enzymes obtained from a fermentation medium from a microorganism of interest. Specifically, Brothers discloses the recovery of alkaline protease and α-amylase from a *Bacillus* culture (see abstract). The enzyme is an extracellular enzyme, specifically proteases, amylases, amyloglucosidases, lipases and oxidases, provided by an enzyme-containing solution produced by the fermentation, in a nutrient growth medium, of enzyme-secreting microorganisms , such as bacteria, yeast or fungi (see column 3, lines 60-68). Further, a precipitation agent, such as a salt or low molecular weight organic solvent, specifically ethylene glycol, is added to the medium (see column 4,lines 12-16, lines 55-61). Preferred salts are ammonium, phosphate and sulfate salts but any Group I or II metal salt is acceptable. A polyol solvent is also added to the fermentation medium to solubilize and recover the enzyme. Polyols may be 100% polyol or a mixture of a polyol and a compatible co-solvent. The polyols comprise low molecular weight polyethylene glycol ,1-2,propandiol, and the C2 through C8 alcohols having atleast two OH groups. C2-C8 alcohols with more than two OH groups may also be used. Such polyols include propylene glycol, glycerol, the low molecular weight (900 or less) polyethylene glycols and mixtures thereof and must be present in the medium of 20% and above (see column 5, lines 3-53). Brothers further discloses organic solvents such as propylene glycol, ethylene glycol and polyethylene glycol may also be used during enzyme

preparation (see column 1, lines 50-53). Given that all compounds in the Markush group as claimed by applicant in claim 14 are polyols, all compounds are anticipated by Brothers et al.

Brothers discloses recovering alkaline protease and alpha-amylase from a 1000 Liter *Bacillus licheniformis* fermentation culture media , wherein the biomass in removed and alkaline protease is recovered after removal of the bacterium (see column 6 , lines 65 continued to column 7 up to lines 56).

Thus, the reference anticipates the claimed subject matter.

The above 102(b) rejection is maintained.

Applicant's arguments filed 10/27/2006 have been fully considered but they are not persuasive. Applicant argues that Brothers does not teach adding a polyol before and/or during the fermentation process, however, applicant defines before and/or after fermentation in the specification , p.6,lines 25-30 as after concentration but before a filtration step. Brothers (col. 4, lines 12-30) teach adding a polyol, specifically a low molecular weight solvent, such as ethylene glycol, to the fermentation solution after concentration, but prior to filtration. Thus, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-31 are rejected under 35 U.S.C. 103(a) as being obvious over Kaasgaard et al (US2004/0175812A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing

that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Applicant claims a method for fermenting a bacterium, specifically *Bacillus* sp., producing an enzyme of interest, specifically a hydrolase, in a culture medium of atleast 50 liters comprising adding one or more compounds in the amount of atleast 0.1%(w/w) selected from 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, mannitol, erythritol, cellobiose, sorbitol and a polyether having an average molecular weight less than 1000, either before and/or during fermentation. Applicant also claims addition of a salt to the medium, such as a chloride, sulphate, phosphate, nitrate, and ammonium salt. The enzyme of interest, a hydrolase, is recovered after removal of the bacterium.

Kaasgaard et al teach a method of recovering a protein of interest by the addition of compounds, specifically polyols and carbohydrates including, trehalose, xylitol, erythritol, sorbitol, monopropylene glycol,i.e. 1,2-propanediol to a bacterial fermentation medium during fermentation wherein an enzyme on interest is recovered (see abstract,0007-0009,0051-0057,0080-0096, claims 1-18) after the removal of the bacterium. They disclose the bacteria to be of the Bacillus genus and the enzyme to be a hydrolase (see 0007-0022). They also teach the addition of salts such as chloride, sulphate, phosphate, nitrate, and ammonium salt (see 0106-0108). The polyol is added in an amount of at least 0.1%(w/w) of medium (see 0093).

Kaasgaard et al do not teach each and every compound, specifically, 1,2 and 1,3-propanediol, arabitol, dulcitol and polyethers with a MW less than 1000. However,

they do teach any polyol having the formula $C_nH_{2n+2}O_n$, and/or a carbohydrate. Thus, the compounds claimed fall within this formula, thus, all the claimed polyols and carbohydrates would be obvious to one of ordinary skill in the art to be added to a fermentation solution to recover an enzyme on interest. Further, as stated in the above 102(e) rejection, propylene glycols, such as 1,2 propandiol are known in the art to be the collective name for monopropylene glycols, thus, 1,2 and 1,3 propandiols would inherently be covered by the term monopropylene glycol.

Claims 14-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brothers et al (U.S. Patent 4,673,647) in view of Schreiber (U.S. Patent 4,016,039) and GB 1001173 and Boyer et al (U.S. Patent 5,385,837).

Applicant claims a method for fermenting a bacterium, specifically *Bacillus* sp., producing an enzyme of interest, specifically a hydrolase, in a culture medium of atleast 50 liters comprising adding one or more compounds in the amount of atleast 0.1%(w/w) selected from 1,2-propandiol, 1,3-propandiol, ethylene glycol, trehalose, xylitol, arabitol, dulcitol, erythritol, sorbitol and a polyether having an average molecular weight less than 1000, either before and/or during fermentation. Applicant also claims addition of a salt to the medium, such as a chloride, sulphate, phosphate, nitrate, and ammonium salt. The enzyme of interest, a hydrolase, is recovered after removal of the bacterium.

As stated above, Brothers et al disclose a process for the recovery of enzymes obtained from a fermentation medium from a microorganism of interest. Brothers differs from the claims in that, although they disclose any polyol and more specifically low

molecular weight polyethylene glycol, 1-2,propandiol, and the C2 through C8 alcohols having atleast two OH groups may also be used. Such polyols include propylene glycol, glycerol, the low molecular weight (900 or less) polyethylene glycols and mixtures thereof, therefore, sugar alcohols such as xylitol, arabitol, dulcitol, erythritol, and sorbitol, may be used during the enzyme preparation. They do not specifically state trehalose, xylitol, arabitol, dulcitol, erythritol, and sorbitol, however, xylitol, arabitol, dulcitol, erythritol, sorbitol and polyethers having an average molecular weight of less than 1000 meet the disclosed characteristics and would therefore be obvious to use such sugar alcohols. It is recognized that Brothers teaches adding a low molecular weight solvent such as ethylene glycol to the fermentation solution before and/or during fermentation as stated above, see col.4, lines 12-30. However, they additionally teach adding a polyol solution, preferably low molecular weight polyethylene glycol,1-2,propandiol, and the C2 through C8 alcohols having at least two OH groups. Such polyols include propylene glycol, glycerol, the low molecular weight (900 or less) polyethylene glycols and mixtures thereof (see column 5, lines 3-53) after fermentation to obtain the enzyme of interest. However, they teach these compounds to be important in obtaining an enzyme of interest in a fermented solution, thus it would be obvious to one of ordinary skill in the art to add these compounds to a fermented composition to obtain a protein, i.e. enzyme during fermentation rather than "after" because these compounds are known in the art to be useful in recovering enzymes in a solution. Thus, one of ordinary skill in the art at the time of the invention would have been motivated to

use polyols disclosed in the art with a reasonable expectation of success in obtaining an enzyme of interest from a fermentation solution.

Further, GB 1001173 discloses a process for the production of galactose oxidase from *Polyporus circinatus Fr.* in an aqueous fermentation medium containing up to 2% (w/v) of a carbohydrate source comprising mannitol, sorbitol, inositol and glycerol (see column 1, lines 36-50 and column 3, lines 10-15). Mineral salts are also desirable in the fermentation medium such as sulphate, nitrate, and ammonium sulphate salts (see column 4, lines 70-80; 104-108). Further support of the use of carbohydrates and salts in a fermentation medium to obtain an enzyme of choice from a microorganism is disclosed by Boyer et al. They disclose obtaining an alkaline protease from *Bacillus proteolyticus* culture containing substrates such as trehalose (see Table 1) and salts such as potassium phosphate, calcium chloride, sodium sulphate and magnesium sulphate (see abstract and column 5, lines 65 continued to column 6, up to lines 56).

Schreiber also disclose a process for the recovery of proteins, specifically proteases, from fermentation solutions containing polyoxyethylene glycol, i.e. polyethylene glycol, having a low molecular weight between 500-800 in the amount of up to 3% by weight and salts such as sulphate and chloride salts(see abstract and column 1, lines 10-13). The polyol is added "during" fermentation, according to applicant's definition of what "before and/or during fermentation" is. Specifically Schreiber teaches adding the polyol to the fermenter solution before precipitation and filtration, i.e, during fermentation.

It is well established that duplicating compounds or components with similar functions within a composition is obvious; see *In re Harza,* 274F.2d 669,124 USPQ 378 (CCPA 1960) and MPEP 2144.04. Polyols, i.e. sugar alcohols were known in the art at the time of the invention to solubilize and recover enzymes (see Brothers et al. column 5,lines 20-27,Schreiber, abstract and col. 1, lines 10-13, GB1001173, and Boyer et al).

One of ordinary skill in the art would therefore have been motivated by the combined disclosures of the references of the addition of many carbohydrates i.e. polyols and sugar alcohols to fermentation mediums during and after fermentation to obtain an enzyme of interest, more specifically the addition of claimed polyols, which are disclosed as being acceptable and successful in a culture medium to obtain enzymes such as hydrolases.

Therefore, the claimed invention as a whole is prima facie obvious over the prior art.

Response to Arguments

Applicant's arguments filed 10/27/2006 have been fully considered but they are not persuasive. Applicant argues that neither reference teaches or suggests adding the claimed polyols to a culture medium before and/or during fermentation in a process of fermenting an enzyme of interest, however, according to applicants explanation of when in the fermentation process comprises before or during, Brothers and Schreiber do teach and suggest adding a polyol/carbohydrate to a fermentation medium during fermentation to obtain an enzyme of interest. Further, although Brothers also suggests adding a polyol to the medium after fermentation, these compounds are known in the art

to be useful in a fermentation medium to obtain an enzyme of interest, thus one of ordinary skill in the art would expect success in adding such a compound to a fermentation before and/or during the fermentation process to obtain an enzyme of interest.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tiffany Gough

RUTH DAVIS
PRIMARY EXAMINER